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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/003,035	WANG, DANHER	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/17/2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *47-98* is/are pending in the application.

4a) Of the above claim(s) *67-76, 78 and 97-98* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47-66 and 77, 79-86 and 94-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *05/28/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment field on December 17, 2003 has been acknowledged. Claims 1-46 and 87-93 have been canceled. New claims 94-98 are added. Claim 47 has been amended. Claims 47-86 and 93-98 are pending.

Election/Restrictions

1. Applicant's election with traverse of group III, claims 47-57, 61-66 and 86 in the species of CMV promoter, HIV clade A and HIA strain BH10 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that claim 47 is a generic claim. Although the specific types or sequences of the HIV antigen have different structures, they share a common genetic character encoded by HIV genome, these HIV antigens are patentable distinct species of the genus HIV antigen. Applicants' argument has been respectfully considered. Group III and IV are rejoined because they are all directed to the envelope protein.

2. Furthermore, upon reconsidering the dependent claims, claims 77, 79, 81, 82, 83, 84 and 94-96 are rejoined with elected group III. However, Group V cannot be rejoined with Group III because it is directed to the gag gene protein and they require different searches as well as exhibit different patentable weights.

3. Claims 47-66 and 77, 79-86 and 94-96 are considered before the examiner.

4. Claims 67-76, 78 and 97-98 are withdrawn from consideration.

Sequence requirements

5. This application contains sequence disclosures in line 25 of pages 16 and line 14 of page 59 that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

6. Full compliance with the sequence rules by **insertion of a sequence identification number (SEQ ID NO)** is required in response to this Office Action. A complete response to this office action should include both compliance with the sequence rules and a response to the

Office Action set forth below. Failure to fully comply with **both** these requirements in the time period set forth in this office action will be held non-responsive.

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

8. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

9. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 47-52, 64, 65, 79-86, 94-96 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 6,544,780B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scopes of claims invention overlapping.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

12. Claims 47, 48, 50, 51, 52, 56, 77, 83, 94, 95, 96 are rejected under 35 U.S.C. 102(a) as being anticipated by Bruce et al. (J. Gene. Virol. 1999, Vol. 80, pp. 2621-2628).

13. Bruce et al. disclose a recombinant bicistronic adenovirus vector made by a replication-deficient adenovirus in which the Rev-responsive element and the envelope glycoprotein gp120 of HIV-1 IIIB strain ranging from nucleotide 5736-8473 were inserted in tandem into the deleted E3 region through splice-donor site and under two powerful cytomegalovirus (CMV) immediate early (IE) promoters respectively. HIV envelope protein and rev proteins are different HIV antigenic proteins, and the Rev protein is also a HIV regulatory protein. Each of them is regulated under a separate CMV promoter (See sections of Methods and Results on pages 2622-2625. Especially see lines 4 to 37 on 1st col. of page 2622 and lines 12 on 1st col. of page 2625 through line 28 on the 1st col. of page 2626 and Fig. 4 on page 2625). Therefore, the claimed invention is anticipated by the cited prior art.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 47, 48, 50, 51, 52, 56, 61-62 64-65, 77, 83 and 94 are rejected under 35 U.S.C. 102(b) as being anticipated by Chanda et al. (Intern. Rev. Immunol. 1999, Vol. 7, pp. 67-77).

16. Chanda et al. dislcose a recombinant adenovirus vector made by adenovirus serotype 7, which comprises an E3 region deletion and an expression cassette containing the entire coding sequence of HIV-1 envelope protein gp160 inserted at the right-hand end of the viral genome between the E4 promoter region and the inverted terminal repeat at the position 159 bp from the extreme right terminus of the Ad 7, and under the control of Ad7 major late promoter (MLP). Furthermore, the HIV rev sequence was inserted in the E3 region under the control of E3 promoter, resulting in the recombinant adenovirus Ad-rev-env (See Fig. 2 on page 70). Because inserted envelope protein contains entire coding sequence of the envelope protein, it inherently

includes a HIV envelope signal peptide and the transmembrane domain of gp41. Therefore, the claims are anticipated by the cited reference.

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. Claims 47, 48, 50, 51, 52, 56 60, 64-66,79-86 and 94-96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chanda et al. (Intern. Rev. Immunol. 1999, Vol. 7, pp. 67-77), Bruce et al. (J. Gene. Virol. 1999, Vol. 80, pages 2621-2628), LaRosa et al. (Science 1990, Vol. 249, pp. 932-935), Ivanoff et al. (US Patent No. 5,141,867A), Gorzigia et al. (J. Virol. 1999, Vol. 73, No. 7, pp. 6048-6055) and Ramshaw et al. (US Patent No. 5,866,131A).

19. Claimed invention is directed to a recombinant bicistronic adenovirus vector made by a replication-incompetent adenovirus comprising two HIV sequences, wherein a first HIV sequence encoding a first HIV antigen, which is expressed under a first promoter; and a second HIV sequence encoding a second HIV antigen, which is under a second promoter control. The HIV antigen can be same or different; and they can be HIV wild type or mutated envelope protein selected from gp160, gp120 or gp41. The first or second HIV sequence can further contain a HIV regulatory sequence selected from Tat, Vif, Nef and Rev.

20. Chanda et al. dislcose a recombinant adenovirus vector made by adenovirus serotype 7, which comprises an E3 region deletion and an expression cassette containing the entire coding sequence of HIV-1 envelope protein gp160 inserted at the right-hand end of the viral genome between the E4 promoter region and the inverted terminal repeat at the position 159 bp from the extreme right terminus of the Ad 7, and under the control of Ad7 major late promoter (MLP). Furthermore, the HIV rev sequence was inserted in the E3 region under the control of E3 promoter, resulting in the recombinant adenovirus Ad-rev-env (See Fig. 2 on page 70). However,

Chanda et al. do not teach to use the adenovirus carrying HIV antigens that are inserted in E1 or E4 region or through an internal ribosomal entry site or via a splicing donor-acceptor mechanism. Chanda et al. teach precisely the inserted envelope protein sequence encoding a V3 loop, a transmembrane domain and a signal peptide.

21. Bruce et al. disclose a recombinant bicistronic adenovirus vector made by a replication-deficient adenovirus in which the Rev-responsive element and the envelope glycoprotein gp120 of HIV-1 IIIB strain ranging from nucleotide 5736-8473 were inserted in tandem into the deleted E3 region through splice-donor site and under two powerful cytomegalovirus (CMV) immediate early (IE) promoters respectively. HIV envelope protein and rev proteins are different HIV antigenic proteins, and the Rev protein is also a HIV regulatory protein. Each of them is regulated under a separate CMV promoter (See sections of Methods and Results on pages 2622-2625. Especially see lines 4 to 37 on 1st col. of page 2622 and lines 12 on 1st col. of page 2625 through line 28 on the 1st col. of page 2626 and Fig. 4 on page 2625). Bruce et al. further teach that the rev provided by bicistronically result in a good expression of HIV envelope protein in vitro and a humoral immune response was detected after two immunizations with the bicistronic recombinant adenovirus vector comprising both envelope and rev proteins (RA142) (See abstract, Figs. 2-4 on pages 2624-2625).

22. Gorzigia et al. disclose that a recombinant adenovirus vector can be constructed with E1, E2a, E3 and all of E4 except open reading frame 3 (See Abstract and Fig. 1 on page 6049), and an insertion of any foreign gene into any of this deleted region can be expressed (See section of RESULTS on pages 6050-6052). They suggest that the additional deletion of E4 on the E1 and E2a deletion background may be beneficial in decreasing immunogenic and improving safety and toxicity profiles, as well as increasing transgene capacity in gene therapy.

23. LaRosa et al. teach a V3 loop of HIV comprising an antigenic fragment with a 100% homology to the SEQ ID NO: 25 as claimed in the current application.

24. Ivanoff et al. (US Patent No. 5,141,867A) teach a transmembrane domain of HIV envelope protein gp41, which has 100% homology to the SEQ ID NO: 75. They also teach this transmembrane domain of HIV gp41 can be used as an antigen to raise a monoclonal antibody (Claims 1-3 and example 2 on col. 7).

25. Murphy et al. disclose a signal peptide (SEQ ID NO: 6) having 100% homology to the claimed signal peptide of SEQ ID NO: 74. They also teach that the use of a heterologous signal peptide fused to a recombinant protein can increase the recombinant protein expression, such as the expression of the recombinant HIV envelope protein gp120 fused with the heterologous signal peptide increase 20-30 folds (See lines 12-42 on col. 15 and lines 18-46 on col. 13).

26. Ramshaw et al. disclose a method for stimulating the immune response of a host by using a preparation of a vaccine vector including adenovirus vector that comprises a first heterologous gene sequence encoding an antigen polypeptide, including HIV-1 antigen polypeptide, and a second heterologous sequence encoding a cytokine selected from a group consisting of IL-1, IL-2, IL-4, IL-5, INF-λ etc. (See claims 1-4, 7, 10-12, 14-17 and lines 62-67 in col. 5).

1. Therefore, in order to produce an enhanced immune response by using a replication-incompetent bicistonic adenovirus vector, it would have been obvious for an ordinary skill person in the art to be motivated to combine all already established knowledge taught by the cited prior art above to construct a replication-incompetent adenovirus vector with E1 and E3 or E4 mutations and express two antigenic sequences with one cytokine sequence with no unexpected result. Because art already established that an adenovirus vector can be made by E1, E3 and/or E4 deletion. Especially, the prior art teaches that the protein expression can be same and with less toxicity if more adenovirus endogenous structural proteins can be deleted because the more endogenous protein is deleted, the less toxicity and vector-induce host immune response can be obtained as reported by Gorigilia et al (See Abstract). All of the claimed sequences are also already known and well described as an antigenic or functional peptide or polypeptide.

2. Hence, the claimed invention as a whole is prime facie obviousness without unexpected result.

Conclusion

Claims 53-55 are free of art rejection. However, they are not in the condition for allowance because they depend on the rejection claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0906. The examiner can normally be reached on 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached at 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao Qun Li
March 16, 2004

James C. Housel 3/22/04
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